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EXAMINER
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ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/419,545	DARJI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9,10 and 17-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10 and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *72005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 07/20/05 has been entered.

Applicants' Amendments

2) Acknowledgment is made of Applicants' amendments filed 07/13/05 and 06/13/05 in response to the final Office Action mailed 03/11/05.

Status of Claims

3) Claim 1 has been amended via the amendment filed 07/13/05.

Claims 11-16 have been canceled via the amendment filed 06/13/05.

Claims 1, 9, 17, 18 and 23 have been amended via the amendment filed 06/13/05.

Claims 1-6, 9, 10 and 17-23 are pending and are under examination.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' information disclosure statement filed 07/13/05 The information referred to therein has been considered and a signed copy is attached to this Office Action.

Prior Citation of Title 35 Sections

5) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

6) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

7) The rejection of claims 18 and 21 made in paragraph 26 of the Office Action mailed 08/11/04

and made or maintained in paragraph 20 of the Office Action mailed 03/11/05 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to claim 18.

8) The rejection of claims 1-6, 9, 10 and 17-23 made in paragraph 21 of the Office Action mailed 03/11/05 under 35 U.S.C. § 112, first paragraph, as being non-enabled, is withdrawn in light of Applicants' amendment to the base claim.

9) The rejection of claim 9 made in paragraph 22(a) of the Office Action mailed 03/11/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

10) The rejection of claim 1 made in paragraph 22(b) of the Office Action mailed 03/11/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

11) The rejection of claim 23 made in paragraph 22(c) of the Office Action mailed 03/11/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claims 2-6, 9, 10 and 17-23 made in paragraph 22(d) of the Office Action mailed 03/11/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

13) The rejection of claims 1, 2, 4-6, 9, 10 and 18-20 made in paragraph 23 of the Office Action mailed 03/11/05 under 35 U.S.C § 103(a) as being anticipated by Branstrom *et al.* (US 5,824,538, filed 09/06/1995) in view of Stocker *et al.* (*Intern. Rev. Immunol.* 11: 167-178, 1994), is withdrawn upon further consideration. A new art rejection is set forth herebelow.

14) The rejection of claim 3 made in paragraph 24 of the Office Action mailed 03/11/05 under 35 U.S.C § 103(a) as being anticipated by Branstrom *et al.* (US 5,824,538, filed 09/06/1995) as modified by Stocker *et al.* (*Intern. Rev. Immunol.* 11: 167-178, 1994) as applied to claims 2 and 1 above, and further in view of Fouts *et al.* (*Vaccine* 13: 1697-1705, 1995, already of record), is withdrawn upon further consideration. A new art rejection is set forth herebelow.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

15) Claim 1 and those dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1, as amended, replaces the limitations: 'a heterologous DNA gene or heterologous gene fragment or an autologous gene or autologous gene fragment' with the new generic limitation: 'a nucleic acid encoding a polypeptide, wherein said nucleic acid'. Applicants state that lines 1 and 2 of page 3, page 3, line 28 through line 18 of page 4, pages 8-10, lines 14-29 of page 14, and page 38 of the specification provide the descriptive support for the added limitations. However, there is no descriptive support in the instant specification, as originally filed, for the full scope of the new limitation 'nucleic acid encoding a polypeptide'. As recited currently, the term 'nucleic acid' encompasses within its scope RNA and a homologous nucleic acid including homologous DNA and RNA, for which there is no support. Therefore, the above-identified limitation in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

It is suggested that Applicants replace the above-identified limitations with --a heterologous gene encoding a heterologous polypeptide, wherein said heterologous gene--.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

16) Claims 1-6, 9, 10 and 17-23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 20 lacks proper antecedent basis and is improperly broadening in scope in the limitation 'of claim 1, wherein *Salmonella* is'. Claim 20 depends from claim 1, which recites

an 'attenuated *Salmonella* strain', but not a generic *Salmonella*. For proper antecedence and clarity, it is suggested that Applicants replace the limitation with --of claim 1, wherein the *Salmonella* strain is--.

(b) Claim 1 is vague in the limitation 'a response', because it is unclear what is encompassed in this limitation. What constitutes a response is not clear. Is this an immune response, non-immune response, reactogenic response, anaphylactic response, allergic response, and/or inflammatory response? Clarification is requested.

(c) Claim 3 lacks proper antecedent basis in the limitation: 'The *Salmonella* strain of claim 2'. Since the strain of claim 2 is specifically 'a *S. typhimurium* strain', it is suggested that Applicants replace the limitation with --The *S. typhimurium* strain of claim 2--.

(d) Claim 5 lacks proper antecedent basis in the limitation 'The *Salmonella* strain of claim 4'. Since the strain of claim 4 is specifically 'a *S. typhi* strain', it is suggested that Applicants replace the limitation with --The *S. typhi* strain of claim 4--.

(e) Claim 6 is vague, indefinite and confusing in the limitation: 'derived' (see line 2), because it is unclear what is encompassed in the limitation 'derived'. Does 'derived' mean isolated, purified, separated, extracted, or recombinantly expressed? Is the vector undergoing any kind of chemical modification or structural alteration during the process of 'deriving'?

(f) Claim 19 is vague, indefinite and has improper antecedence in the limitation: 'the vertebrates are'. Claim 19 depends from claim 1, which recites 'a vertebrate', but not 'vertebrates'.

(g) In claims 9 and 23, it is suggested that Applicants delete the '-' following the limitations: '*coli*' and/or '*monocytogenes*'.

(h) Claims 2-6, 9, 10 and 17-23, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

17) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this

subsection based on the filing of an international application filed under the treaty defined in section 351(a).

18) Claims 1, 2, 4, 6, 9, 10 and 17-22 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Powell *et al.* (US 5,877,159, filed 05/03/1995 – Applicants' IDS).

The term 'vaccine' in claim 10 represents the intended use of the claimed strain and therefore is not given any patentable weight.

Powell *et al.* ('159) disclosed an attenuated bacterium having a eukaryotic expression cassette comprising a foreign gene that expresses a vaccine antigen in mammals including humans, in levels sufficient to induce an immune response. The eukaryotic expression cassette is expressed by the infected cells and progeny thereof. Powell's ('159) invention does not involve delivery of prokaryotic expression cassettes to and expression of the foreign antigen by the bacterial vaccine vector in animal cells or tissues. In contrast, it involves the delivery of eukaryotic expression cassettes, including plasmids such as p-beta-gal+SV plasmid containing a viral derived CMV eukaryotic promoter, by bacterial strains to cells in animal tissue and expression *in vivo* of the eukaryotic expression cassettes by the animal cells in animal tissue in the intact animal of the family mammalian, pisces, or avian. See abstract; fourth and fifth full paragraphs in column 6; claims 15-24; lines 15-19 in column 25; first paragraph in column 23; and line 59 in column 7; and the last paragraph in column 7. Powell *et al.* ('159) expressly taught that their invention provides the first documentation of genetic exchange between live invasive bacteria and animal cells (see fifth full paragraph in column 6). The bacterium used is attenuated *Salmonella* species (see claim 18 and fourth full paragraph in column 10). The *Salmonella* strain used is attenuated *Salmonella typhi* or attenuated *S. typhimurium.* The particular *Salmonella* strain employed is not critical to the invention (see second full paragraph in columns 13 and 14). The invasive bacteria containing the eukaryotic expression cassettes encode a tumor-specific antigen, a transplant antigen, an auto-immune antigen (see first full paragraph in column 18), viral, bacterial or parasitic protein vaccine antigen (see last three paragraphs in column 16). The administration is by oral route (see second and fifth full paragraphs in column 19). That the attenuation in the prior art *Salmonella* strain is suitable 'for vaccination of a vertebrate' including a human is inherent from the teachings of Powell *et al.* ('159). The capability of the encoded polypeptide to induce an antibody response and a T-cell

response as recited in claims 17, 18, 21 and 22 is viewed as an inherent property inseparable from the prior art product. Since the prior art product meets the recited structural features, the prior art strain is expected to have the recited capability to induce an antibody response and a T-cell response. The Office's position that the prior art strain meets Applicants' attenuated *Salmonella* strain is based upon the fact that every characteristic overlapping in Powell's ('159) strain and Applicants' strain are the same. There is sufficient overlap between the two strains to reasonably conclude that Powell's ('159) strain anticipates Applicants' strain. Since the Office does not have the facilities for examining and comparing Applicants' attenuated *Salmonella* strain with the prior art strain, the burden is on Applicants to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the attenuated *Salmonella* strain of the prior art does not possess the same functional characteristics of the claimed attenuated *Salmonella* strain). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

Claims 1, 2, 4, 6, 9, 10 and 17-22 are anticipated by Powell *et al.* ('159).

Rejection(s) under 35 U.S.C. § 103

19) Claim 3 is rejected under 35 U.S.C § 103(a) as being unpatentable over Powell *et al.* (US 5,877,159, filed 05/03/1995 – Applicants' IDS) ('159) as applied to claims 2 and 1 above, and further in view of Fouts *et al.* (*Vaccine* 13: 1697-1705, 1995, already of record).

The teachings of Powell *et al.* ('159) are described above, which do not expressly disclose the *S. typhimurium* strain to be SL7207 or *S. typhi* Ty21a.

However, the attenuated *aroA S. typhimurium* SL7207 vaccine strain was known and available in the art at the time of the invention. For instance, Fouts *et al.* taught the attenuated *aroA S. typhimurium* SL7207 vaccine strain specifically for expressing a heterologous antigen to elicit a heterologous antigen-specific immune response in a vertebrate (see abstract; Figure 5; and pages 1698, 1700, 1702, and page 1703, right column).

Given the express teaching of Powell *et al.* ('159) that *S. typhimurium* strain is used in their invention and that the particular *Salmonella* strain employed is not critical to the invention, it would have been *prima facie* obvious to one of ordinary in the art at the time the invention was made to replace the generic *S. typhimurium* vaccine strain in Powell's ('159) vaccine with Fouts'

attenuated *aroA S. typhimurium* SL7207 vaccine strain to produce the instant invention with a reasonable expectation of success. Replacement of one art known *S. typhimurium* vaccine strain with another alternative, art known attenuated *S. typhimurium* vaccine strain such as Fouts' SL7207, for the same purpose of eukaryotic expression of a heterologous antigen in a vertebrate was well within the realm of routine experimentation, would have been obvious to one of ordinary skill in the art, and would have produced similar results or effects absent evidence to the contrary.

Claim 3 is *prima facie* obvious over the prior art of record.

20) Claim 5 is rejected under 35 U.S.C § 103(a) as being unpatentable over Powell *et al.* (US 5,877,159, filed 05/03/1995 – Applicants' IDS) as applied to claim 1 above, and further in view of Dyall-Smith *et al.* (US 5,332,658).

The teachings of Powell *et al.* ('159) are described above, which do not expressly disclose the *S. typhi* strain to be Ty21a.

However, the attenuated *S. typhi* Ty21a vaccine or vector strain was known and available in the art at the time of the invention. For instance, Dyall-Smith *et al.* taught the use of *S. typhi* Ty21a vaccine or vector strain specifically for expressing a heterologous gene to elicit a heterologous protein-specific immune response in a vertebrate (see last paragraph in column 2).

Given the express teaching of Powell *et al.* ('159) that *S. typhi* strain is used in their invention and that the particular *Salmonella* strain employed is not critical to the invention, it would have been *prima facie* obvious to one of ordinary in the art at the time the invention was made to replace the generic *S. typhi* vaccine or vector strain in Powell's ('159) vaccine with Dyall-Smith's *S. typhi* Ty21a strain to produce the instant invention with a reasonable expectation of success. Replacement of one art known *S. typhi* vaccine or vector strain with another alternative, art known attenuated *S. typhi* vaccine strain such as Dyall-Smith's *S. typhi* Ty21a strain for the same purpose of expression of a heterologous antigen in a vertebrate was well within the realm of routine experimentation, would have been obvious to one of ordinary skill in the art, and would have produced similar results or effects absent evidence to the contrary.

Claim 5 is *prima facie* obvious over the prior art of record.

Remarks

21) Claims 1-6, 9, 10 and 17-23 stand rejected.

22) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses or papers is (571) 273-8300.

23) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see,http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

24) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

September, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER